Perioperative reliability of an on-site prothrombin time assay under different haemostatic conditions

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Abstract: Perioperative use of laboratory coagulation assays is limited by the delay in obtaining results. The management of haemostasis during major surgical procedures requires rapid and accurate measurement of the prevailing coagulation status. In this prospective study, we have evaluated the reliability of on-site prothrombin time assessed by the portable coagulation monitor CoaguChek-Plus compared with standard laboratory assays during elective non-cardiac surgery. Sixty-two patients were assigned to one of three groups: group A = normal preoperative coagulation where minor intraoperative blood loss is expected; group B = normal preoperative coagulation where major intraoperative blood loss is expected; and group C = preoperative anticoagulation and minor intraoperative blood loss expected. On-site prothrombin time and laboratory prothrombin time showed poor correlation in group A (r2 = 0.24; bias (2 SD) 1.80 (3.34) S) and group B (r2 = 0.30; 1.43 (3.12) S). The correlation in group C was better (r2 = 0.71; 1.41 (1.92) S). We conclude that prothrombin time measured with the CoaguCheck-Plus monitor did not appear to be suitable for the management of haemostasis.

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Summary

Perioperative use of laboratory coagulation assays is limited by the delay in obtaining results. The management of haemostasis during major surgical procedures requires rapid and accurate measurement of the prevailing coagulation status. In this prospective study, we have evaluated the reliability of on-site prothrombin time assessed by the portable coagulation monitor CoaguChek-Plus compared with standard laboratory assays during elective non-cardiac surgery. Sixty-two patients were assigned to one of three groups: group A = normal preoperative coagulation where major intraoperative blood loss is expected; and group B = normal preoperative coagulation where minor intraoperative blood loss is expected; and group C = preoperative anticoagulation and minor intraoperative blood loss expected. On-site prothrombin time and laboratory prothrombin time showed poor correlation in group A ($r^2 = 0.24$; bias (2 SD) 1.80 (3.34) s) and group B ($r^2 = 0.30$; 1.43 (3.12) s). The correlation in group C was better ($r^2 = 0.71$; 1.41 (1.92) s). We conclude that prothrombin time measured with the CoaguChek-Plus monitor did not appear to be suitable for the management of haemostasis. (*Br. J. Anaesth*. 1998; **81**: 533–536).

Keywords: blood, coagulation; blood, haemostasis; measurement techniques, coagulation

Intraoperative assessment of coagulation is of major concern, as it may alter rapidly during surgery as a result of both major blood loss and volume replacement with colloids, crystalloids and blood components.[1] Furthermore, an increasing number of patients with compromised haemostatic potential present for surgery. The prothrombin time (PT) assay is used in the perioperative period as a routine measure of the extrinsic pathway of coagulation. The clinical use of most laboratory coagulation assays, including PT, continues to be restricted by the delay in obtaining results. Rapid determination of PT may be helpful in the case of major bleeding and coagulopathy. Despotis and colleagues demonstrated that the use of on-site coagulation assays can reduce the use of blood products, decrease operating time and minimize chest tube drainage in cardiac surgery.[2]

The portable coagulation monitor CoaguChek-Plus (Boehringer Mannheim, Germany, formerly Biotrack 512, Ciba-Corning, Medfield, MA, USA) has been shown to measure accurately intraoperative on-site PT in less than 3 min.[3 4] Comparison of results with those of standard laboratory assays has been made in cardiac[2–5] and gynaecological surgery.[6] The purpose of our prospective study was to evaluate the reliability of CoaguChek-Plus prothrombin time (CC-PT) in comparison with simultaneous standard laboratory prothrombin time (LAB-PT) assays under different haemostatic conditions during elective non-cardiac surgery.

Patients and methods

After obtaining approval from the Ethics Committee and informed patient consent, we studied 62 patients with no history of bleeding. Patients were allocated to one of three groups: group A = normal preoperative coagulation and minor intraoperative blood loss expected; group B = normal preoperative coagulation and major intraoperative blood loss expected; and group C = preoperative oral anticoagulation with phenprocoumon (Marcoumar) or acenocoumarol (Sintrom), discontinued before surgery, or high-dose i.v. heparin. The inclusion criterion for those receiving oral anticoagulants was a laboratory PT < 65% (corresponding to an international normalized ratio (INR) of > 1.4) on the day before surgery. The inclusion criterion for patients receiving heparin was a daily dose of heparin > 15 000 u. (Liquemin). Assessment of PT was performed on 3–5 separate occasions: (1) before operation, after induction of anaesthesia; (2) during operation, up to three times, depending on the length of the surgical procedure and amount of blood loss and fluid replacement; and (3) after operation, before patient transport from the operating theatre to the recovery room or intensive care unit.

CC-PT measurements were performed strictly in accordance with the manufacturer's instructions. The technical and methodological aspects of the CoaguChek-Plus monitor have been described by Lucas and colleagues.[7] All blood samples were obtained from a non-heparinized central venous catheter, the catheter being rinsed with 20 ml of saline beforehand. 10 ml of blood were withdrawn and discarded before sampling. For the CoaguChek-Plus, one drop of the sampled blood was applied immediately to the inserted CC-PT cartridge. For the

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Table 1 Perioperative packed cell volume (PCV) and intraoperative blood transfusion (mean (SD)). CC-PT = CoaguChek-Plus prothrombin time (PT) measurements; LAB-PT = laboratory PT measurements. $^{**}P<0.01$, $^{***}P<0.001$, significant differences in group B compared with both groups A and C

	Group A	Group B	Group C
Number of comparisons (CC-PT *vs* LAB-PT)	138	37	16
Preoperative PCV (%)	37.1 (7.1)	34.7 (10.6)	39.2 (3.9)
Postoperative PCV (%)	30.9 (6.7)	23.4 (3.7)**	31.2 (3.8)
Packed red blood cells transfused (ml)	820 (496)	2160 (684)***	350

standard laboratory assay, 10 ml of whole blood were drawn up into a citrate-containing glass tube and sent immediately to the laboratory. LAB-PT measurements were performed using the Electra 1600 C (Medical Laboratory Automation, Pleasantville, NY, USA) and thromboplastin Innovin (DADE Behring, Illinois, USA). The INR, calculated by the CoaguChek-Plus monitor, was compared with the INR of the laboratory assay.

STATISTICAL ANALYSIS

Comparisons between groups (packed cell volume (PCV), units of transfused blood) were made using analysis of variance (ANOVA) and the Bonferroni–Dunn test. Possible trends in the differences in consecutive measurements were analysed by ANOVA for repeated measures with the Greenhouse–Geisser correction. The correlation between CC-PT and LAB-PT measurements was determined by linear regression and bias analysis. $P<0.05$ was considered statistically significant. The statistical program used was Stat View for Windows v. 4.57 (Abacus Concepts Inc.) running on an IBM personal computer.

Results

PCV values before and after operation and packed red blood cell requirements are shown in table 1. Preoperative PCV was similar in all groups. Group B had a significantly higher intraoperative need for packed red blood cells. After operation, following blood product use, PCV in group B was significantly lower than that in the two other groups.

Immediate preoperative PT measurements were similar in all groups. There was an over-reading (bias) of 1.41 s (group C) to 1.80 s (group A) in CC-PT compared with LAB-PT (fig. 1). CC-PT and LAB-PT correlation values (r^2) were 0.24, 0.30 and 0.71 in groups A, B and C, respectively (fig. 2). Expression of PT as INR (logarithmic scale) did not improve the correlation between CC-PT and LAB-PT, with r^2 values of 0.12, 0.12 and 0.73 for groups A, B and C, respectively. Extreme outliers in group A and B are apparent in figures 1 and 2.

There was no trend in the accuracy between measurements before, during and after operation for all groups. Furthermore, accuracy was similar for normal (PT <13.5 s) and abnormal (PT ≥ 13.5 s) ranges of PT. Most of the abnormal PT values were found in group B.

Discussion

We found only a weak correlation between prothrombin time measured with the CoaguChek-Plus monitor and that measured in the laboratory. Several outliers contributed substantially to the poor accuracy of the device. In several cases the difference in LAB-PT and CC-PT was 10–16 s. Thus the CoaguChek-Plus monitor indicated an abnormal PT when a normal PT was verified by standard laboratory testing and clinical judgement. These false pathological PT values may lead to unnecessary and potentially harmful substitution therapy with blood products. There were no outliers in group C, but the probability of outliers occurring was limited because of the low number of comparisons (16 *vs* 138 and 37 for groups A and B, respectively). Accordingly, the best correlation was found in this group. The poor accuracy of the device was found equally for measurements before, during and after operation, and for different ranges of PT.

In view of the small number of outliers, it might be

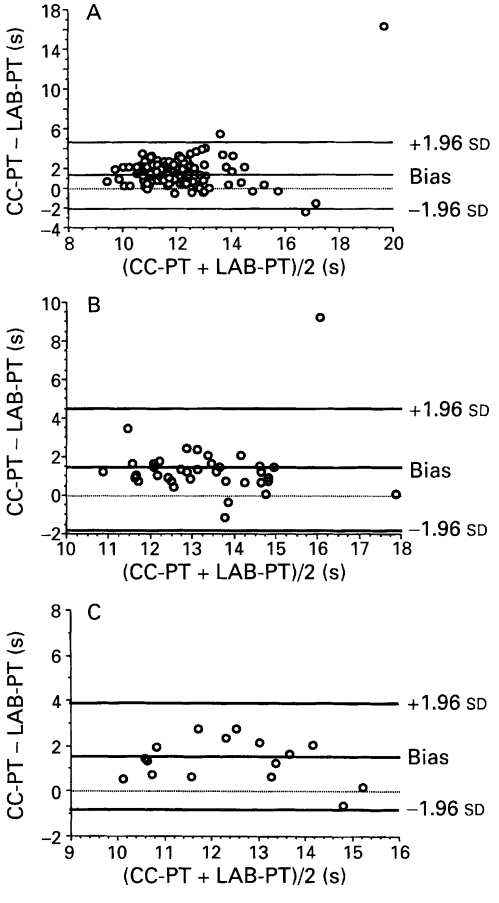

Figure 1 Bland Altman plot showing bias (mean of differences) and precision (1.96 SD of these differences) of prothrombin time obtained by the CoaguChek-Plus monitor (CC-PT) compared with prothrombin time measured with standard laboratory assays (LAB-PT) in group A ($n=138$; A), group B ($n=37$; B) and group C ($n=16$; C), respectively.

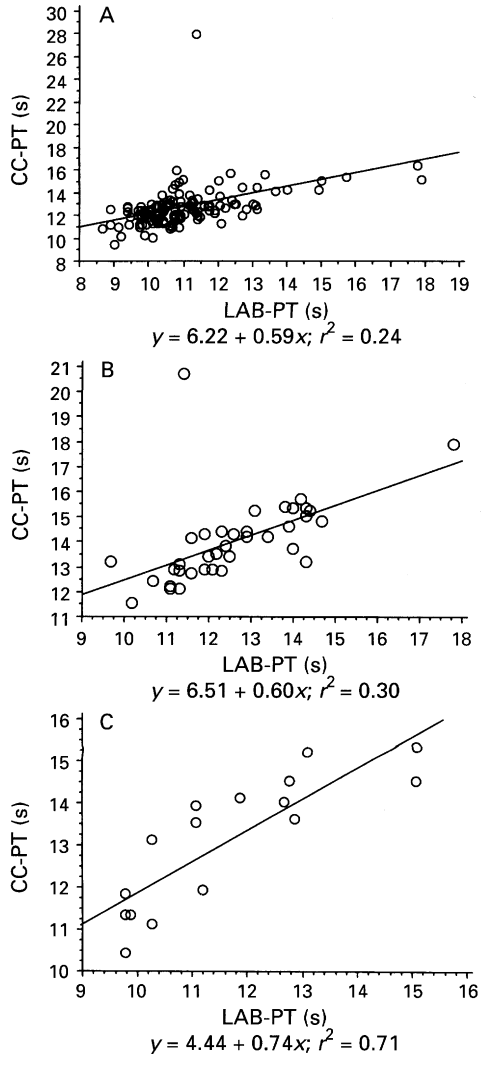

Figure 2 Equations of regressionl ines and plots of linear regression showing prothrombin time measured using standard laboratory assays (LAB-PT) compared with prothrombin time obtained by the CoaguChek-Plus monitor (CC-PT) for groups A (A), B (B) and C (C).

argued that technical or handling errors may have been responsible for inaccurate measurements. However, blood sampling, measurements and calibration were performed carefully by the investigators in strict accordance with the recommendations of the manufacturer. Moreover, in daily clinical practice, an on-site coagulation monitor should be easily and reliably used by theatre staff.

The accuracy of measurement of PT with the CoaguChek-Plus coagulation monitor has been validated in a wide range of medical specialities, such as clinical pathology,[7–9] haematology,[10] cardiac surgery[2–5] and gynaecological surgery.[6] Most studies showed acceptable accuracy in comparison with standard laboratory methods. Jennings, Luddington and Baglin evaluated the CoaguChek-Plus for the control of oral anticoagulation.[8] They compared several thromboplastins, including lyophilized rabbit brain thromboplastin used in the CoaguChek-Plus monitor with the "consensus" (mean of all compared INR) within the therapeutic range for oral anticoagulation. The results showed a clinically and statistically significant overestimation by the CoaguChek-Plus monitor. The authors concluded that the CoaguChek-Plus would be suitable for decentralized anticoagulant monitoring, but should not be used when laboratory testing with standard thromboplastin is available.

The international sensitivity index (ISI), which has a logarithmic relationship to INR, describes the individual sensitivity of a thromboplastin compared with the WHO (World Health Organisation) reference thromboplastin. Tripodi and colleagues determined the ISI and precision of the INR of the CoaguChek-Plus monitor compared with the secondary international WHO reference preparation for rabbit thromboplastin.[10] ISI was 2.715, which is higher than that adopted by the manufacturer (2.036), and also higher than the laboratory thromboplastin of our study (0.96). The authors suggested that the poor correlation of INR may be caused by the high ISI. They also recommended the use of more sensitive thromboplastins with lower ISI values because these show smaller between-laboratory variability. This argument may also explain the worsening of the correlation we found in groups A and B after expressing PT as INR units. Nevertheless, for comparison of PT values, INR is the only relevant parameter.[11 12] In accordance with Tripodi and colleagues, we would prefer a more sensitive thromboplastin for on-site PT measurement.

Despotis and colleagues[3] and Reich and colleagues[5] reported an acceptable accuracy for the CoaguChek-Plus monitor in cardiac surgery compared with laboratory standard assays. Samama and colleagues also found good correlations in vascular and gynaecological surgery.[6] In contrast, Nuttal and colleagues found only moderate correlation with laboratory assays in their study of 100 patients undergoing cardiopulmonary bypass.[4] These authors concluded that "speeding access" to hospital laboratory results would be a more efficacious alternative.

In contrast with previous work, we performed repeated measurements in individual patients. Furthermore, the reliability of the CoaguChek-Plus monitor was evaluated under various haemostatic conditions. Its accuracy may suffice for the control of oral anticoagulation,[7–9] but our results indicate that CoaguChek-PT measurements are not reliable enough for clinical decision making in non-cardiac surgery.

During elective aortic replacement surgery, even laboratory PT has been shown to be unreliable for assessing coagulation status.[13] Within the past decade, thrombelastography has become a useful adjunct to intraoperative haemostasis management, enabling a global assessment of haemostatic function.[14] Together with the processes of clot formation, clot strengthening and clot lysis, even platelet function can be determined.[15 16] The various thrombelastographic variables correlate closely with intraoperative coagulopathy and enable selective substitution of blood products in accordance with the specific requirements of the case.[17] If indicated, an accurate platelet count may also be obtained on-site.[3]

In summary, we advise against the use of the CoaguChek-Plus coagulation monitor to evaluate the patient's prevailing prothrombin time or to monitor changes during non-cardiac surgery. The associated time-saving effect does not compensate for the lack of reliability. Perioperative haemostasis management should be based primarily on good clinical judgement

and reliable coagulation testing, such as is provided by laboratory coagulation status, when indicated in combination with on-site platelet count, on-site activated clotting time or thrombelastography.[1 3 14–16]

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